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PATENT & TRADEMARK OFFICE

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PATENT
Customer No. 22,852
Attorney Docket No. 06478.1452-00

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re Application of:	)	
	)	
Hubert METZNER et al.	)	Group Art Unit: 1654
	)	
Application No.: 09/809,021	)	Examiner: Michael V. Meller
	)	
Filed: March 16, 2001	)	
	)	
For: THROMBIN PREPARATIONS AND PROCESS FOR THEIR PRODUCTION	)	Confirmation No.: 5147

Mail Stop Appeal Brief--Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

REPLY BRIEF UNDER 37 C.F.R. § 1.193

Appellants now reply to the Examiner's Answer, mailed July 29, 2004, to the Appeal Brief in this application, filed May 19, 2004.

Three copies of this Reply Brief are filed herewith.

I. Issues

A. Whether claims 18-19 and 35-38 are novel under 35 U.S.C. § 102(b) over Allary et al. (abstract).

B. Whether claims 18-19 and 35-38 are novel under 35 U.S.C. § 102(b) over Lorne et al. (abstract).

C. Whether claims 18-19 and 35-38 are nonobvious under 35 U.S.C. § 103(a) over Allary et al. or Lorne et al., taken with Hanada et al., Brezniak et al., and Altshuler.

Full citations for each of those publications are provided at page 3 of the Examiner's Answer, as well as in the Appeal Brief. Translations of the full text of Allary et al. and Lorne et al. are attached to the Examiner's Answer.

The Appeal Brief filed May 19, 2004, lists several other grounds of rejection in addition to those above. However, the Examiner's Answer states, at pages 3-4, that only the three grounds of rejection listed above "are applicable to the appealed claims." Appellants' understanding is that all other grounds of rejection have been withdrawn, as the Examiner's Answer does not comment on them. *See* M.P.E.P. § 1208, 8th Ed., May, 2004 revision, paragraph bridging pages 1200-17 and 1200-18.

II. Grouping Of Claims

Claims 18-19 and 35-38 stand or fall together. See the Appeal Brief, filed May 19, 2004.

III. Argument

A. Claims 18-19 and 35-38 Are Novel over the Abstract of Allary et al.

Appellants' claim 18 recites two components and a functional requirement for the preparation as a whole. It requires thrombin and a "noncovalently binding inhibitor of thrombin activity" in a preparation that, as a whole, is "suitable for therapeutic purposes," meaning that it can be directly administered to a patient. Claim 18 could only be anticipated by a single reference that expressly or inherently teaches every limitation of that claim, including the functional limitation. *See, e.g., Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987); M.P.E.P. § 2131.

The Examiner maintains his contention that the abstract of Allary et al. anticipates claim 18. (Examiner's Answer at page 4.) The abstract states only: "[w]e used one affinity chromatography [stage] on benzamidine-Spherodex and compared three methods of elution" including elution with "biospecific competitors (arginin[e] methylester or benzamidin[e])." This suggests a solution eluted from a chromatography column containing thrombin and benzamidine. But it teaches nothing at all about therapeutic safety.

Indeed, in the Answer, the Examiner continues to side-step around the functional requirement of "suitability for therapeutic purposes." First, the Examiner asserts that the specification does not clearly define that phrase. (Examiner's Answer at page 5.) Yet, the specification repeatedly illustrates its meaning. For example, at page 1, second paragraph, the specification points out that "[t]he precondition for use of thrombin for medical purposes is that it can be made available to the clinician as a stable product

which has high virus safety and contains minimal amounts of inactive byproducts or degradation products of thrombin or other factors." At page 3, first full paragraph, the specification comments that the prior art does not provide "a purified, calcium ion-containing, virus-safe thrombin preparation . . ." Thus, Appellants sought "a simple and improved process . . . for using high-purity thrombin with high virus safety." (Specification at page 3, last two lines.) Further, the specification emphasizes the need for virus safety throughout its description of the process used to produce the preparations according to this invention. (*See, e.g.,* page 4, final paragraph, and page 5, second full paragraph, and Example 4 at pages 9-10.) In contrast, Allary's abstract teaches nothing regarding the specific safety, purity, and stability requirements of the instant claims.

As a second way to avoid the requirement of therapeutic suitability, the Examiner comments that "the references teach thrombin preparations which are going to be used for" therapeutic purposes at some later stage. (Examiner's Answer at page 5.) However, the eventual fate of Allary's final thrombin solution is simply irrelevant to this § 102 rejection because it doesn't contain any inhibitor. The issue here is solely whether or not the intermediate that does contain the inhibitor meets the requirements of claim 18.

The full text of Allary, a translation of which the Examiner has now placed of record, shows that Allary does not anticipate claim 18. For example, Allary teaches that the intermediate solution containing the inhibitor "is dialyzed or ultrafiltered in NaCl 1 M medium" and then dialyzed again before it is placed "final form" for eventual use. (See the translation of Allary et al., attached to the Examiner's Answer, at page 5.) By this

process, the buffer is changed and all traces of the inhibitor are removed before any therapeutically suitable thrombin solution is actually obtained. Thus, Allary teaches that the intermediate solution is *not* "suitable for therapeutic purposes."

Finally, the Examiner contends that Appellants are "making the preparation the same way as the references are," alleging that the preparations therefore must be the same. (Examiner's Answer at page 5.) Yet the main similarity is simply that both methods include chromatography, which is a general laboratory technique encompassing a wide variety of discreet methods, and is used in the purification of nearly every known species of protein. Thus, this statement only serves to obscure the differences in the two procedures.

For example, the instant application teaches methods of making a highly pure and virus safe preparation of thrombin and a noncovalently binding inhibitor of thrombin activity. The text at pages 4-5 and Examples 1-4, for instance, shows that cation exchange chromatography and hydrophobic interaction chromatography are conducted along with at least one viral inactivation process. To form the final preparation, the inhibitor is added separately. In contrast, Allary's abstract teaches a different type of chromatography, called affinity chromatography, which uses a thrombin competitor as one of its ingredients. Allary's full text teaches that this affinity chromatography stage is an intermediate step and that one should dialyze or ultrafiltrate the intermediate, then dialyze again, to remove the inhibitor from the thrombin before a "final form" is made. (Translation of Allary et al. at page 5.) Thus, the two solutions are not prepared by the same procedures and are not the same.

For these reasons, Appellants request the Board to overturn this rejection.

B. Claims 18-19 and 35-38 Are Novel over the Abstract of Lorne et al.

The abstract of Lorne et al. appears to Appellants essentially duplicative of that of Allary et al. For that reason, Appellants' arguments in Section A above apply equally here, and are not re-stated.

Further, the Examiner now places a translation of the full text of Lorne et al. of record. (Translation attached to Examiner's Answer.) That full text teaches that "the final recovery of this thrombin obtained by chromatography [i.e., the eluate containing the inhibitor] must be done via a preliminary dialysis or ultrafiltration in an NaCl 1 M medium in order to dissociate the complex formed with the elution agent [i.e., the inhibitor]." (Translation of Lorne et al., attached to Examiner's Answer, at page 15.) Thus, Lorne et al. even more strongly teaches that the inhibitor must be removed from the thrombin solution, and that the inhibitor-containing intermediate is not "suitable for therapeutic purposes."

Thus, Appellants request the Board to overturn this rejection.

C. Claims 18-19 and 35-38 Are Nonobvious over Allary et al. or Lorne et al., taken with Hanada et al., Brezniak et al., and Altshuler

The Examiner bases the obviousness rejection on his contention that Allary and/or Lorne anticipate the instant claim 18. (Examiner's Answer at pages 4 and 6.) Appellants illustrate above, however, that Allary and Lorne do not anticipate claim 18. In fact, they also teach away from it, by teaching that dialysis or ultrafiltration are needed to remove the inhibitor before making any therapeutically suitable solution. (Allary et al., translation at page 5; Lorne et al., translation at page 15.) For example, Lorne et al. teaches that "the final recovery of this thrombin obtained by

chromatography must be done via a preliminary dialysis or ultrafiltration in an NaCl 1 M medium in order to dissociate the complex formed with the elution agent [i.e. the inhibitor]." (Translation, attached to Examiner's Answer, at page 15.)

Moreover, even if, *arguendo*, Allary or Lorne could inherently anticipate any of Appellants' claims, they still could not render the claims obvious. Inherency is "quite immaterial to [an obviousness rejection] if . . . one of ordinary skill in the art would not appreciate or recognize the inherent result." *In re Rijckaert*, 9 F.3d 1531, 1533, 28 U.S.P.Q.2d 1955, 1957 (Fed. Cir. 1993). Indeed, it cannot be obvious to modify a property that the art does not recognize or know. In this case, regardless of the Examiner's contentions, Allary and Lorne themselves evidently believed that their intermediate was not "suitable for therapeutic purposes," because their articles teach those of ordinary skill in the art to remove the inhibitor and change the buffer before obtaining a usable thrombin solution. (See Examiner's Answer at page 4.) The Examiner did not consider these teachings of Allary and Lorne.

The Examiner also asserts that he cites Hanada, Brezniak, and Altshuler solely for their teachings about extra ingredients, such as those recited in claim 19. (Examiner's Answer at page 6.) But in doing so, he fails to consider those publications as a whole. For example, Appellants pointed out in the Appeal Brief that Hanada teaches away from the present invention in the same way as Allary and Lorne. (Appeal Brief at pages 19-22.) It teaches using an inhibitor only at an intermediate treatment stage and removing it before making a therapeutically suitable thrombin solution. (*Id.*) The Examiner contends that Brezniak uses calcium chloride and that the use alone is sufficient motivation to combine Brezniak with the other cited art. (Examiner's Answer

at page 6.) But the Examiner does not consider Brezniak's conclusion that sodium chloride is a better stabilizer. (Appeal Brief at paragraph bridging pages 22 and 23, and citations therein.) Thus, Brezniak does not motivate one of ordinary skill in the art to choose calcium when sodium is freely available. (*Id.*) The Examiner also contends that Altshuler does not teach away from the instant claims. (Examiner's Answer at page 6.) However, Appellants merely explained that Altshuler's teachings are restricted to dry or powdered preparations and do not apply, for example, to claim 19, which recites a thrombin preparation that is "stable in the liquid state." (*Id.*; and see Appeal Brief at page 23, lines 3-8.)

Courts have long held that an Examiner may not pick and choose elements from a reference that support a rejection, while ignoring others that do not support the rejection. *See, e.g., In re Wesslau*, 353 F.2d 238, 241, 147 U.S.P.Q. 391, 393 (C.C.P.A. 1965); *Bausch & Lomb, Inc. v. Barnes Hind/Hydrocurve, Inc.*, 796 F.2d 443, 448-9, 230 U.S.P.Q. 416, 420 (Fed. Cir. 1986). Yet this picking and choosing is exactly what the Examiner does here. Instead, the Examiner must consider the teachings of the cited art as a whole, including any teaching away. *See EWP Corp. v. Reliance Universal, Inc.*, 755 F.2d 898, 907, 225 U.S.P.Q. 20, 25 (Fed. Cir. 1985) ("A reference must be considered for everything it teaches by way of technology and is not limited to the particular invention it is describing and attempting to protect. On the issue of obviousness, the combined teachings of the prior art as a whole must be considered.") Because the Examiner does not consider the teachings of Allary, Lorne, Hanada, Brezniak, and Altshuler as a whole, he has not made a *prima facie* case of obviousness. Thus, Appellants request the withdrawal of this rejection.

Appellants respectfully request the entry of this Reply. If any fees are required to enter this brief, please charge such fees to Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: September 28, 2004

By: _____
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